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Cytokine profile in response to Chikungunya virus (CHIKV) associated with CHIKV polyarthritis in acute febrile patients from South India

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Background: Chikungunya causes an acute febrile illness with painful syndrome, asthenia, skin rash, and polyarthritis. In some cases polyarthralgia can last for months to year. Understanding cytokine profile in CHIKV may be helpful to determine severity of the severity.

Methods & Materials: Acute phase blood samples were collected from CHIKV suspected cases during an outbreak in northern districts of Kerala in 2008 and 2009. Samples were processed and stored at -80^{0}C. All the collected samples were screened by CHIKV RT-PCR targeting E2 region (305bp). Among 237 samples collected from an outbreak, 30 chikv suspected samples (20 PCR positives and 10 PCR negatives) and 10 healthy controls were tested with cytokine ELISA. IL-6, IL-8, IL-10, TNF-α and IFN-γ single analyte cytokine quantification ELISA were performed.

Results: Among 237 collected during the outbreak, 51 (21.5%) samples were confirmed as CHIKV by RT-PCR. Majority the patients with severe joint pain was much higher in 2009 (85%) than in 2008 (26%). Joint pain was found more among chikv PCR positive patients when compare to CHIKV PCR negatives (p = 0.04) and it was statistically significance. Cytokines detection ranged from 13.28-72.32pg/ml, mean- 16.4 for IL-6, 7.65-322.01pg/ml, mean-84.57 for IL-8, 24.99-109.8pg/ml, mean- 8.23 for IL-10, 51.35–277.48pg/ml, mean-75.66 for TNF-α, and 49.95– 166.71pg/ml, mean-78.3 for IFN-γ. IL-8, IL-6 and IFN-γ were found to be elevated among chikv patients when compare to control (p=0.00001, 0.004 and 0.005) respectively and it was statistically significance. TNF-α and IL-10 were not significantly increased (p=0.09, p=0.16). Majority of the patients (96%) reported with joint pain shown increased level of IL-8. New vector adaptability of CHIKV may cause for the severity of joint pain during outbreak.

Conclusion: Determination of specific immune mediators involved in the disease progression may be helpful for therapeutic interventions. IL-8 may be used as early biomarker for CHIKV infection to understand severity of the disease.

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Elucidation of viral load and host immune responses as severity predictors of acute lower respiratory tract infections (ALRTI) mediated by respiratory syncytial virus (RSV) and human metapneumovirus (hMPV)

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Background: RSV and hMPV are the most significant causes of severe lower respiratory tract infections with high mortality in children under 2 years of age worldwide. Disease pathogenesis is yet to be ascertained however host immune mechanisms and viral load might play some role. The present study is undertaken to explore the correlating factors in terms of RSV & hMPV load and host immune responses to predict the ALRTI severity

Methods & Materials: NPAs were collected from children (n=142) admitted in PGIMER, Chandigarh with ALRTI from December 2014-October 2015. Samples positive for RSV and hMPV by RT PCR targeting N gene were subjected for viral load estimation by Real Time PCR using CDC recommended primer-probes. The level of IL-17A, IFN-γ, TNF- α, IL-10, IL-6, IL-4 & IL-2 in NPA samples were determined in flow cytometry by cytokine bead array. The viral load and cytokine levels were correlated with the WHO guidelines of ALRTI severity determination. The statistical significance was calculated with SPSS 16.0

Results: Of the 142 patients, 74(52.1%) presented with bronchiolitis, 63(44.5%)with pneumonia and 5(3.3%)with Wheezing. 51 patients (35.91%) were classified under ALRTI, 63 (44.36%) severe ALRTI and 28 (19.71%) very severe ALRTI. RSV and hMPV positivity were seen in 56 (39.42%) and 14 (9.85%) patients respectively. Bronchiolitis was the most common clinical presentation (55.4%) in RSV infected children. RSV viral load amounting to 2.75X 10^5, 1.22X10^5 and 1.16X10^5/ μl of 500ng RNA were seen in ALRTI, severe ALRTI and very severe ALRTI patients respectively (p=0.613). The mean value of IL-17A in RSV infected very severe ALRTI patients was 144.38pg/ml followed be 115.65pg/ml in severe ALRTI and 80.40 pg/ml in ALRTI groups. IL-10 level in very severe ALRTI with RSV was 714.1 pg/ml whereas 132.90 pg/ml in severe ALRTI patients. The mean value of cytokines in hMPV patients were found to be as 171.43pg/ml (IL-6), 334.82 pg/ml (IL-10), 23.14pg/ml (TNF-α), 100.46pg/ml (IFN-γ) and 86.33 pg/ml (Il-17).

Conclusion: Future study involving large group of patients to elucidate viral factors and immune markers as a predictor of severity will be extremely helpful for ALRTI management and disease intervention

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